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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/840,861	04/25/2001	Daniel Dupret	58763.000013	4902

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EXAMINER	
HASHEMI, SHAR S	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 09/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/840,861	Applicant(s) DUPRET ET AL.	
	Examiner Shar Hashemi	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *37-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-36* is/are rejected.

7)☒ Claim(s) *1-36* is/are objected to.

8)☒ Claim(s) *1-41* ~~are~~ have been subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10/19/01* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *9* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 1-36, drawn to process of creating a recombinant polynucleotide sequence, classified in class 435, subclass 91.1.

   II. Claims 37-39, drawn to recombinant polynucleotide sequence, classified in class 536, subclass 23.1

   III. Claim 40, drawn to protein, classified in class 514, subclass 2.

   IV. Claim 41, drawn to bank of sequences, classified in 435, subclass 6.

2. The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the recombinant polynucleotide sequence as claimed in Invention II can be made by a materially different process such as DNA shuffling.

Inventions I and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects MPEP § 806.04, MPEP § 808.01). In the instant case the different

inventions Group I is drawn to a process of creating a recombinant polynucleotide sequence used in hybridization technology whereas Group III is drawn to a protein used in antibody production.

Inventions I and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions Group I is drawn to a process of creating a recombinant polynucleotide sequence whereas Group IV is drawn to a bank used in computer based programs.

Inventions II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions Group II is drawn to a process of creating a recombinant polynucleotide sequence used in hybridization technology whereas Group III is drawn to a protein used in antibody production.

Inventions II and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions Group II is drawn to a recombinant polynucleotide sequence used in hybridization technology whereas Group IV is drawn to a bank used in computer based programs.

Inventions III and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects MPEP § 806.04, MPEP § 808.01). In the instant case the different

inventions Group III is drawn to a protein used in antibody production whereas Group IV is drawn to a bank which may be used in computer based programs.

Because these inventions are distinct for the reasons given above and the search required for each group is not required for the other groups, restriction for examination purposes as indicated is proper.

During a telephone conversation with Mr. David Milligan on September 3, 2002, a provisional election was made without traverse to prosecute the invention of Group I, claims 1-36. Affirmation of this election must be made by applicant in replying to this Office action. Claims 37-41 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Information Disclosure Statement

3. The information disclosure statement filed on 7/30/02 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Drawings

4. The drawings are objected to because Figures 1-6 lack descriptions. Each figure must correspond to a description. A proposed description of drawing correction or corrected drawing descriptions are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Specification

5. The abstract of the disclosure is objected to because the title of the section (i.e "ABSTRACT OF THE DISCLOSURE") is missing. Correction is required. See MPEP § 608.01(b).

6. The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC (See 37 CFR 1.52(e)(5) and MPEP 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text are permitted to be submitted on compact discs.) or
REFERENCE TO A "MICROFICHE APPENDIX" (See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.)
(e) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.

(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.

(f) BRIEF SUMMARY OF THE INVENTION.

(g) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).

(h) DETAILED DESCRIPTION OF THE INVENTION.

(i) CLAIM OR CLAIMS (commencing on a separate sheet).

(j) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).

(k) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use. The lettered items that appear in bold are missing section headings.

Claim Objections

7. Claims 4-10, 22, & 29-30 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

8. Claims 1 & 11 are objected to because of the following informalities: The term "matrix" can be deleted since it is understood that in the context of the claim, "matrices" would be inclusive of a single "matrix." Delete "matrix" and remove the parenthesis around matrices. Appropriate correction is required.

9. Claims 1-3, 11-21, 23-28 and 31-36 are objected to because of the following informalities: The term "method" is more conventional U.S. drafting language. Replace "process" with "method." Appropriate correction is required.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-36 are indefinite because the method steps are confusing in claims 2, 3, 11, 12, 14, 15, 17-21, 23-25, 27, 28, & 31-35. It is unclear as to whether the method steps reflect the preamble. The method steps must be rewritten with **active steps** (e.g. fragmenting).

B) Claims 1-36 are indefinite because the term "it" is confusing in claims 1-3 & 11-13. It is unclear as to whether the term "it" refers to the process of making a recombinant polynucleotide sequence or another process.

C) Claims 18-24 & 29-36 are indefinite because the term "and/or" is confusing in claims 18-20 & 23. The metes and bounds of these claims cannot be established because the parameters that determine "and" is different from the parameters that determine "or."

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 1-3, 11-18, 20, 24-28 and 31-36 are rejected under 35 U.S.C. 102(e) as being anticipated by Stemmer et al (US 2001/0049104 A1 December 6, 2001).

Stemmer et al in US 2001/0049104 A1 teach a method of making a recombinant polynucleotide sequence comprise cutting the bank of polynucleotide sequences to create fragments, denaturing the fragments, hybridizing the fragments to assembly matrices, performing oriented ligation on the fragments to obtain recombinant polynucleotide sequences, separating the recombinant polynucleotide sequences from the assembly matrices, amplifying the recombinant polynucleotide sequences, cloning the recombinant polynucleotide sequences, selecting recombinant polynucleotide sequences that offer advantageous characteristics compared to corresponding characteristics of reference sequences (pages 12-13, paragraphs 118-124; page22, paragraph 196).

They further teach in the cutting step randomly treating the bank of polynucleotide sequences with DNAase I to produce fragments which are used as matrices in the hybridizing and ligating steps (page 13, paragraph 123). They teach in the cutting step the initial bank is fragmented into n fragments where n fragments being greater than or equal to 3 (page 13, paragraph 122-126). They teach the initial bank of polynucleotide sequences is produced from a wild gene by successive steps of controlled mutagenesis (page 14, paragraph 131). They teach the bank of polynucleotide sequences consists of synthetic sequences that will be fragmented (page 9, paragraph 91). They further teach in the cutting step that restriction enzymes are used to

hydrolyze polynucleotides sequences of the bank where the sequences have numerous cutting sites (pages 17-18, paragraph 158) . They teach random fragmentation of the polynucleotide sequences are performed by an enzymatic method (page 13, paragraph 123). They teach the initial bank of polynucleotide sequences consists of several restricted banks prepared by the previously mentioned process (page 13, paragraph 123).

They further teach that the hybridizing step can occur adjacent to the fragment ends on the assembly matrices prior to performing oriented ligation on the fragments. They teach single-stranded of varying lengths are added in the hybridizing step (page 22, paragraphs 196-199). They also teach the hybridizing and ligating steps are performed simultaneously (page 14, paragraphs 128-133). They teach in the hybridizing step, single-stranded exonucleases recognize, degrade, and cut the nonhybridized ends of the fragments when these ends cover other hybridized fragments on the matrix (page 14, paragraph 127-128).

They further teach in the ligating step obtaining recombinant polynucleotide sequences and optionally cloning those sequences that offer advantageous characteristics compared with the corresponding characteristics of reference sequences (pages 16-18, paragraphs 144-168). They teach in the separating step a marker located on the assembly matrix facilitates the separation of the recombinant polynucleotide sequences from the assembly matrix (page 22, paragraph 196-199). Finally, they teach screening is performed by *in vitro* expression of recombinant polynucleotide sequences (pages 9-10, paragraphs 96-98).

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stemmer et al (US 2001/0049104 A1 December 6, 2001) in view of Prudent et al (US 6348314 February 19, 2002).

The teachings and suggestions have been discussed previously.

Stemmer et al in US 2001/0049104 A1 do not teach flap endonuclease.

Prudent et al in US 6348314 teach Flap endonuclease (col. 6, lines 47-65).

One of ordinary skill at the time the invention was made would have been motivated to apply Prudent et al's US 6348314 Flap endonuclease to Stemmer et al in US 2001/0049104 A1 method of making a recombinant polynucleotide sequence in order to cleave nucleic acids at internal sites (col. 23, lines 53-67). It would have been prima facie obvious to apply Prudent et al's US 6348314 Flap endonuclease to Stemmer et al in US 2001/0049104 A1 method of making a recombinant polynucleotide sequence in order to cleave nucleic acids at internal sites (col. 23, lines 53-67).

14. Claims 21 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stemmer et al (US 2001/0049104 A1 December 6, 2001) in view of Auerbach (US 5614389 A March 25, 1997).

The teachings and suggestions have been discussed previously.

Stemmer et al in US 2001/0049104 A1 do not teach thermostable ligases that are active at high temperatures. They also do not teach the thermoresistance and high temperature properties of the ligase are similar to the exonuclease that is used in the hybridizing step.

Auerbach in US 5614389 A teaches thermostable ligases that are active at high temperatures (col. 28, lines 1-20). He also teaches the thermoresistance and high temperature properties of the ligase are similar to the exonuclease that is used in the hybridizing step (col. 28, lines 1-20).

One of ordinary skill at the time the invention was made would have been motivated to apply Auerbach's US 5614389 A thermostabile ligases to Stemmer et al in US 2001/0049104 A1 method of making a recombinant polynucleotide sequence in order to ligate strands (col. 11, lines 25-32). It would have been prima facie obvious to apply Auerbach's US 5614389 A thermostabile ligases to Stemmer et al in US 2001/0049104 A1 method of making a recombinant polynucleotide sequence in order to ligate strands.

SUMMARY

15. No claims allowed. Claims 1-36 rejected to under 35 U.S.C. 112 2nd, claims 1-3, 11-18, 20, 24-28, 31-36 are rejected to under 35 U.S.C. 102(e), claims 19, 21, & 23 are rejected to under 35 U.S.C. 103(a) while claims 4-10, 22, 29-30 are objected to under 37 CFR 1.75(c) and have not been further treated on the merits.

CONCLUSION

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shar Hashemi whose telephone number is (703) 305-4840 and whose e-mail address is shar.hashemi@uspto.gov. However, the Office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner is on flex-time schedule and can be best reached on weekdays from 7:00 a.m. to 3:30 p.m. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119.

Any inquiry of a general nature, matching or filed papers or relating to the status of this application or proceeding should be directed to the Sharon Thornton for Art Unit 1637 whose telephone number is (703)-305-3001.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Center numbers for Group 1600 are Voice (703) 308-1235 and Before Final FAX (703) 872-9306 or After Final FAX (703) 308-9307.

September 4, 2002

JEFFREY SIEW
PRIMARY EXAMINER
9/17/02